REMARKS

Claim Amendments

Claim 47 is amended to recite a recombinant adenovirus comprising a mutated HIV envelope protein. Various HIV envelope protein mutations were disclosed in page 47, line 21 to page 49, line 18.

Claim 53 is amended to recite mutating gp160 protein by deleting the cleavage site between gp120 and gp41. Support for this claim can be found at page 77, lines 26-28.

Claims 54-55 are amended to recite the recombinant adenovirus of claim 53 further comprises a deletion in the C-terminal cytosolic domain of gp160. Support for these claims can be found at page 78, lines 7-13.

Claims 57-59 are amended to recite HIV envelope protein comprising variable loops that are heterologous to a native progenitor of the recombinant adenovirus. Support for such mosaic HIV antigen can be found at page 50, lines 3-26.

Claim 77 is amended to recite mutating HIV envelope protein by deleting the V1 region, V2 region, or V1 and V2 regions. Support for this claim can be found at page 48, lines 20-25.

Sequence Requirement

Sequence identification numbers (SEQ ID NO) have been added to pages 16 and 59 as requested by the Examiner.

Obviousness-Type Double Patenting Rejection

Claims 47-52, 64, 65, 79-86 and 94-96 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent 6,544,780. This rejection is respectfully traversed.

U.S. Patent 6,544,780 describes a recombinant adenovirus comprising (1) sequence encoding a first viral antigen and a second viral antigen that are expressed bicistronically under the control of a first promoter, and (2) an immuno-stimulator

sequence under the control of a second promoter. In contrast, the present invention is drawn to a recombinant adenovirus comprising (1) a first HIV sequence encoding a mutated HIV envelope protein under the transcriptional control of a first promoter, and (2) a second HIV sequence encoding a second HIV antigen under the transcriptional control of a second promoter. Applicant submits that the present invention is patentably distinct from U.S. Patent 6,544,780. Accordingly, Applicant respectfully requests that the double patenting rejection of 47-52, 64, 65, and 79-86 be withdrawn.

Rejections Under 35 USC §102(a)

Claims 47, 48, 50-52, 56, 77, 83, 94-96 are rejected under 35 USC §102(a) as anticipated by **Bruce** et al. This rejection is respectfully traversed.

Bruce et al. describe a replication-deficient adenovirus expressing the envelop glycoprotein gene *env* of HIV-1. More specifically, **Bruce** et al. teach a bicistronic adenovirus vector expressing HIV-1 *rev* and *env* in tandem. **Bruce** et al. only teach wild-type HIV antigen. In contrast, the present invention is drawn, *inter alia*, to recombinant adenovirus comprising mutated HIV envelope protein such as gp160, gp120 or gp41. **Bruce** et al. do not teach or suggest an adenoviral vector comprising mutated HIV antigen. Hence, **Bruce** et al. do not teach or suggest each and every aspect of the present invention. Accordingly, Applicant respectfully requests that the rejection of claims 47, 48, 50-52, 56, 77 and 83 under 35 U.S.C. §102(a) be withdrawn.

Rejections Under 35 USC §102(b)

Claims 47, 48, 50-52, 56, 61-62, 64-65, 77, 83, 94 are rejected under 35 USC §102(b) as anticipated by **Chanda** et al. This rejection is respectfully traversed.

Chanda et al. describe an adenovirus vector expressing HIV-1 *rev* and *env*. More specifically, **Chanda** et al. teach inserting the *rev* gene in the E3 region under the control of E3 promoter, and inserting the *env* gene in another expression cassette under the control of another promoter. **Chanda** et al., however, only describe using wild-type HIV antigen. In contrast, the present invention is drawn, *inter alia*, to recombinant adenovirus comprising mutated HIV envelope protein such as gp160, gp120 or gp41. **Chanda** et al.

do not teach or suggest an adenoviral vector comprising a mutated HIV antigen. Hence, **Chanda** et al. do not teach or suggest each and every aspect of the present invention. Accordingly, Applicant respectfully requests that the rejection of claims 47, 48, 50-52, 56, 61-62, 64-65, 77, 83 under 35 U.S.C. §102(b) be withdrawn.

Rejections Under 35 USC §103(a)

Claims 47, 48, 50-52, 56, 60, 64-66, 79-86, 94-96 are rejected under 35 USC §103(a) as being unpatentable over **Chanda** et al., **Bruce** et al., **LaRosa** et al., **Ivanoff** et al., **Gorzigia** et al. and **Ramshaw** et al. This rejection is respectfully traversed.

Chanda et al. and **Bruce** et al. are discussed above. **Gorzigia** et al. describe an adenoviral vector lacking E1, E2a, all of E4 except open reading frame 3, and expressing a b-galactosidase reporter gene. **Gorzigia** et al. do not describe or suggest any HIV antigen. **LaRosa** et al. describe sequences of the third variable region of gp120. **Ivanoff** et al. describe a sequence encoding a transmembrane domain of HIV gp41. **Murphy** et al. describe a signal peptide for expression of secretory protein. **Ramshaw** et al. describe using recombinant vaccinia virus vector as vaccine.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations (M.P.E.P §2143). Applicant submits that the Examiner has failed to establish a *prima facie* case of obviousness because the combined prior art references do not teach or suggest all the claim limitations.

The present invention is drawn, *inter alia*, to a recombinant adenovirus comprising mutated HIV envelope protein such as gp160, gp120 or gp41. Claimed mutations include mutating gp160 protein by deleting the cleavage site between gp120 and gp41; deleting the C-terminal cytosolic domain of gp160; inserting heterologous variable loops into HIV envelope protein; and deleting the V1 region, V2 region, or V1 and V2 regions of HIV envelope protein. The cited prior art, however, do not teach or suggest any

mutation related to HIV envelope protein gp160, gp120 or gp41. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure (M.P.E.P §2143). Applicant submits that at best, one skilled in the art might find it obvious to try various combinations of the elements culled from these references. However, "obvious to try" is not the standard of 35 U.S.C. §103

In view of the above remarks, the invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicant respectfully requests that the rejection of claims 47, 48, 50-52, 56, 60, 64-66, 79-86 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed March 24, 2004. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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